

## **REMARKS**

Claims 1-27 are pending in the application.

Claims 6-7, 15-16 and 24-25 are amended above to overcome the examiner's indefiniteness rejection.

Claims 19-27 are amended above to overcome the examiner's Section 101 rejection.

Many of the claims are also amended above to clarify what the Applicant regards as the invention.

Claims 2, 5, 7, 11, 14 and 16 are amended to convert them into independent form.

All claims have been amended to define the acronyms ER and PR.

No new matter has been added to the application by way of these specification and claim amendments.

### **I. THE CLAIM OBJECTIONS**

Applicants thank the examiner for the suggestion regarding defining ER and PR in the independent claims, and this has been implemented in the amended claims submitted herewith.

### **II. THE SECTION 112, SECOND PARAGRAPH REJECTION**

Claims 6, 7, 15, 16, 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in view of the expression "a first contribution thereto".

Applicants have amended these claims to recite "a first contribution to an ER or PR score" and "a second contribution to the ER or PR score".

### **III. THE SECTION 101 REJECTION**

Claims 19-27 are rejected under 35 U.S.C. 101 for being directed to non-statutory subject matter.

The examiner's rejection is overcome by amending claims 19-27 above to direct them to "A computer software product comprising a computer readable hardware medium containing computer readable instructions for controlling operation of computer apparatus" either by containing this phrase or by depending from a claim that contains it. This limitation is based on Applicants' specification at page 18 lines 25-26, repeated here for convenience: "The carrier

medium may be a memory, a floppy or compact or optical disc or other hardware recordal medium”.

#### IV. THE ANTICIPATION REJECTION

The examiner rejected claims 1, 3, 4, 6, 10, 12, 13, 15, 19, 21, 22, 24 under 35 U.S.C. 102(e) as being anticipated by US 2003/0165263 to Hamer et al. ("Hamer").

Regarding claim 1, the examiner states that Hamer discloses a method of scoring Oestrogen and Progesterone Receptors expression (ER and PR) from image data obtained from histological slides by determining the number of relatively dark image pixels compared to relatively bright image pixels and scoring ER or PR in accordance with the magnitude of that number of relatively dark pixels. In this connection the examiner's rejection relies upon the teaching found a pages 8-9, paragraph 196, 198-201 of Hamer where it is taught that “the ratio of sufficiently brown pixels to the total number of pixels is determined and used to score ER and PR”.

Applicants have amended claim 1 to distinguish it more clearly over Hamer by defining the number of relatively dark image pixels as being those having intensities below a predetermined intensity threshold. As the examiner acknowledges in his reasons for allowing certain application claims, Hamer does not use an intensity threshold. Instead Hamer transforms to the Hue/Saturation/Value (HSV) image space (V= intensity), ignores V and uses a hue modulus threshold and two saturation thresholds. H and S are derived from Equations (7) to (10) on page 8 of Hamer as follows:

$$\sin \phi = \frac{\tilde{x}y - x\tilde{y}}{\sqrt{\tilde{x}^2 + \tilde{y}^2} \sqrt{x^2 + y^2}} \quad (7)$$

$$\cos \phi = \frac{x\tilde{x} + y\tilde{y}}{\sqrt{\tilde{x}^2 + \tilde{y}^2} \sqrt{x^2 + y^2}} \quad (8)$$

$$\phi = \sin^{-1} \frac{|\tilde{x}y - x\tilde{y}|}{\sqrt{\tilde{x}^2 + \tilde{y}^2} \sqrt{x^2 + y^2}} \quad (9)$$

$$\text{saturation } S = \frac{x\tilde{x} + y\tilde{y}}{\tilde{x}^2 + \tilde{y}^2} \quad (10)$$

Hamer's Table 1 on page 8 is then used to convert  $\phi$  to  $\psi$  in the range 0 to  $\pi/2$ , and a hue threshold  $\psi_0$  is set equal to 80 degrees or  $4\pi/9$ . By inspection of Hamer's Equation (10), saturation  $S = 1$  when the pixel coordinates  $(x, y)$  are equal to the reference colour coordinates  $(\tilde{x}, \tilde{y})$  in the chromaticity space 58 (fig. 5).  $S$  will be small or large compared to 1 when one or both of the chromaticity space pixel coordinates are far from those of the reference colour. The two saturation threshold values for  $S_0$  are  $S_0 = 0.9$  for  $S$  differing by not more than 0.9 from 1, i.e.  $S$  in the range 0.1 to 1.9, and  $S_0 = 0$  for  $S$  differing by more than 0.9 from 1, i.e.  $S$  outside the range 0.1 to 1.9.

Now Hamer page 8 paragraph 190 states that the reference colour "is the colour of that part of the image which is most positively stained (the most intense colour on the part of the original slide from which the image was taken)". The saturation of a pixel outside the range 0.1 to 1.9 is therefore much smaller or much larger than the saturation  $S = 1$  of a pixel having the most intense colour in the image, and a pixel outside the range 0.1 to 1.9 will still be counted as a brown pixel in the brown pixel total  $N_b$  by Hamer so long as  $S$  is greater than 0 (see Table 2 on page 8). Moreover, a pixel inside the range 0.1 to 1.9 will also be counted in the brown pixel total  $N_b$  if it has saturation  $S = 0.9$  or above, i.e. if it is at least 90% of the reference colour saturation  $S = 1$ : a pixel counted in the brown pixel total  $N_b$  can therefore have the same saturation as the reference colour saturation  $S = 1$  for the most intense colour in the image. Consequently, saturation and intensity are not the same thing, and, contrary to the examiner's remarks, Hamer does not count relatively dark (i.e. low intensity) pixels to get sufficiently brown pixels. Moreover, as noted above, claim 1 is amended herein to define the number of relatively dark image pixels as being those having intensities below an intensity threshold which Hamer does not disclose. For at least this reason, independent claim 1 is novel and patentable.

Claims 10 and 19 are respectively computer apparatus and software product claims which correspond to method claim 1. Claims 10 and 19 have been amended equivalently to claim 1 and are novel and patentable for the same reasons recited above with respect to claim 1.

Claims 3, 12 and 21 have been amended similarly to claims 1, 10 and 19 to define the number of relatively dark image pixels as being those with intensities below an intensity threshold which Hamer does not disclose. Claims 3, 12, and 21 are novel for at least this reason.

Regarding claims 4, 13 and 22, the examiner appears to have overlooked the fact that an image contains background pixels in addition to blob pixels. (See Applicants' specification at page 13 lines 22-23). Consequently, Applicants' invention as claimed in claims 4, 13 and 22 is clearly novel over Hamer, because Hamer includes background pixels but claims 4, 13 and 22 exclude them. In other words, Hamer counts brown pixels  $N_b$  and total image pixels  $N$  (which includes background pixels) to give  $N_b/N$ . (See Hamer paragraph 198 pages 8-9, page 9 line 2 in particular). In contrast, Applicants' invention counts brown blob pixels and total blob pixels (which excludes background pixels). To emphasise this Applicants have amended claims 4, 13 and 22 above to specify that the image data comprises pixels corresponding to blobs and pixels corresponding to background.

The dependency of claims 6, 15 and 24 is amended above to correct an error that would otherwise result in methods and apparatuses that count relatively dark pixels twice. Turning now to the rejection of claims 6, 15 and 24, it is the examiner's position that paragraphs 197-199 of Hamer discloses "average saturation is determined, divided by the number of sufficiently brown pixels and scored". The examiner's position is incorrect. In paragraph 197 Hamer discloses determining average saturation by adding together the saturation values  $S$  of the  $N_b$  sufficiently brown pixels and dividing by  $N_b$ ; that average is then divided by the maximum saturation of those pixels to give a normalised percentage saturation: it is this normalised percentage saturation (not average saturation) which is "scored", i.e. compared with percentage ranges to give a first score contribution. (See last sentence of paragraph 197). A second score contribution (see Table 5 page 9) then comes from the ratio  $N_b/N$  of brown pixels  $N_b$  and total pixels  $N$  (including background pixels). The two score contributions are then added together. As has been said above in detail in relation to claim 1, saturation and intensity are not the same thing and Hamer does not count relatively dark (i.e. low intensity) pixels to get sufficiently brown pixels. Moreover, claims 6, 15 and 24 have been amended to define the number of relatively dark image pixels as being those having intensities below a predetermined intensity threshold which Hamer does not disclose. For at least these reasons, claims 6, 15 and 24 are also novel over Hamer.

**V. THE ALLOWABLE SUBJECT MATTER**

Applicants note that claims 8, 9, 17 and 18 are allowed and thanks the examiner in this regard.

Claims 2, 5, 11 and 14, which the examiner objected to for depending upon a rejected claim, are rewritten above to convert them into independent form including all of the limitations of the relevant base claim and any intervening claims in each case, and are now believed to be allowable.

Claims 7 and 16 have been rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph and to include all of the limitations of the relevant base claim and any intervening claims in each case, also as indicated by the examiner to be allowable.

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By: /A. Blair Hughes/  
A. Blair Hughes  
Reg. No. 32,901  
312-913-2123  
hughes@mbhb.com